REMARKS

Newly added claims 30-35 are pending in the Application. Claims 6-18, 21, 22 and 24-29 were canceled herein. Applicants respectfully submit that the new claims are supported by the specification and original claims. Accordingly, no new matter has been added.

The pending claims have not been rejected. However, the new claims correspond approximately to several of the rejected (and canceled) claims, as indicated below:

Claim 30 corresponds approximately to claims 12 and 14.

Claim 31 corresponds approximately to claim 13.

Claim 32 corresponds approximately to claim 15.

Claim 33 corresponds approximately to claim 16.

Claim 34 corresponds approximately to claim 17.

Claim 35 corresponds approximately to claim 18.

In view of the above, and in order to advance prosecution, Applicants address the rejections in the Office Action as they may be applied to the newly submitted claims.

The title of the application was also amended to reflect proper English usage of the adjective "therapeutic."

Applicants respectfully submit that the claims are in condition for allowance and earnestly solicit notification to that effect.

Rejection under 35 U.S.C. § 101

The Office Action indicates that claims 24 and 25 are directed to unpatentable subject matter under 35 U.S.C. § 101. Claims 24 and 25 have been canceled herein, thereby mooting the rejection.

Rejection under 35 U.S.C. § 112, first paragraph- Enablement

The Office Action indicates that claims 6-18, 21-22 and 24-29 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enabling support in the specification. Applicants respectfully traverse the rejection inasmuch as it may be applied to the new claims.

The Examiner has acknowledged that the specification enables inhibiting IL-8 in vitro and treating sepsis. However, the Examiner alleges that the specification "does not reasonably provide enablement for the treatment and prevention of any and all diseases associated with IL-8, i.e. Gerhardt disease and ischemia-reperfusion injury." (Office Action at page 3). In support of this allegation, the Examiner asserts: 1) "the ability of preventing... diseases associated with IL-8, i.e. sepsis and ischemia reperfusion injury is not yet known in the art"; 2) the specification

does not provide guidance as to how one of skill in the art can prevent the diseases; 3) there are no working examples showing prevention of the diseases can be achieved or a protocol for assessing efficacy. The Examiner concludes that the amount of experimentation required of the skilled artisan to prevent the listed diseases by way of the present invention would be undue. Thus, the gravamen of the rejection is understood to be that the Examiner doubts that the invention could be used to prevent any of the conditions listed in the claims.

At the outset, Applicants respectfully remind the Examiner that the Patent Office has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 999 F.2d 1557, 1562 (Fed. Cir. 1993). A specification which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. MPEP 2164.04.

Applicants respectfully assert that the specification provides ample enabling support for how to make and use the pharmaceutical compositions of the invention as claimed, i.e., methods for treating or preventing a disease or disorder associated with suppression of neutrophil apotosis or excessive release of IL-8. For example, the specification describes the pool of patients to which the invention pertains, i.e., those suffering from inflammatory diseases mediated by excessive neutrophil accumulation resulting in tissue damage. (See page 5, lines 14-17 and listing of treatable disorders at pages 14-15). Applicants have described a small genus of compounds, identified by formulas I, II and III, which are suitable for use in the claimed methods, and have provided information regarding how to obtain the compounds. (See, e.g., page 11, lines 5-8). Applicant has described suitable dosing regimens and routes of administration. (See page 13, lines 18-21). Applicants have provided *in vitro* and *in vivo* models, in working examples, with which to assess treatment effects of the compositions of the invention for septicemia and acute respiratory distress. (See pages 19-35). In other words, Applicant has clearly and concisely instructed in sufficient detail how to practice the claimed invention. As stated above, there is a presumption of correctness as to Applicant's disclosure that the Examiner has not rebutted. As noted above, the burden lies with the Examiner to provide a reasonable basis for questioning Applicants' disclosure.

The Examiner states, without support, that "the term 'prevention' or 'preventing' is synonymous with the term 'curing' and both circumscribe methods of treatment having absolute success." To the contrary, at least one definition of "prevention" is "any activity which reduces

the burden of mortality or morbidity from disease." As shown in the attached Wikipedia definition (Exhibit 1), there are three levels of prevention known in medicine: primary, secondary and tertiary. As stated in Exhibit 1, "Tertiary prevention reduces the negative impact of an already established disease by restoring function and reducing disease-related complications." In view of this definition, Applicants assert the enabling support in the specification is sufficient under 35 U.S.C. § 112, first paragraph.

Moreover, Riedemann et al., cited in the Office Action, is not as unequivocal as the Examiner implies. The Office Action states that this reference concludes that the 'silver bullet' for treating sepsis has not yet been found. However, Riedemann et al. also indicate that inhibitors of apoptosis have been found to be beneficial in animal models. (Riedemann et al. at page 346, col. 2) Riedemann et al. further state, "in the case of a hyper-reactive immune system, an anti-inflammatory strategy is more likely to be beneficial." (Riedemann et al. at page 346, col. 2). Thus, far from negatively portraying the potential for therapies such as Applicants' claimed invention, Riedemann et al. expresses hope that a viable treatment may be discovered.

As noted above, Applicants respectfully assert that the invention as claimed is enabled by the specification. However, in order to advance prosecution and address the Examiner's concerns regarding use of the term "preventing" in the claims, Applicants respectfully submit the Declaration of Dr. Dong-Keun Song under 37 CFR 1.132 ("Song Declaration," or "the Declaration"). As described in the Declaration, an experiment was conducted to demonstrate the ability of 1-steroyl LPC to prevent sepsis in an animal model. Specifically, as indicated in the Declaration:

> Fifteen BALB/c mice (each weighing about 25-30 g) were divided into three groups of five. Each group of five was injected subcutaneously with either 10 mg/kg of 1-stearoyl LPC, 20 mg/kg of 1-stearoyl LPC or fatty-acid free 1% bovine serum albumin (BSA) solution (control) fifteen minutes before injecting $5x10^8$ bacteria into the abdominal cavity of the mice. After 8 hours, the number of peritoneal bacteria remaining was estimated.

(Song Declaration, paragraph 7).

> As explained by Dr. Song, the results of this experiment show that:
>
> the number of bacteria cleared by BALB/c mice, in colony forming units (CFU ($x10^5$)) per unit volume of peritoneal fluid, after pre-treatment with 1-stearoyl LPC (10 mg/kg or 20 mg/kg) was significant in comparison to that of the control (BSA) group.

(Song Declaration, paragraph 8 and Exhibit B).

Dr. Song concludes from the data that 1-stearoyl LPC was effective in preventing sepsis in vivo. (Song Declaration, paragraph 8). According to Dr. Song, the data presented in the Declaration support the statements in the specification that the claimed compositions have the ability to prevent sepsis. (Song Declaration, paragraph 9). Moreover, Dr. Song states:

> Based on the evidence provided herein and in the specification, a worker in the field would expect that these results could be extrapolated to the other diseases or disorders recited in the claims, based on their common etiologies, i.e., suppression of neutrophil apoptosis and/or excessive release of IL-8.

(Song Declaration, paragraph 9).

In view of the above and the Declaration of Dr. Song submitted herewith, Applicants respectfully request withdrawal of the enablement rejection under 35 USC §112, first paragraph.

Rejection under 35 U.S.C. § 112, first paragraph- Written Description

The Office Action indicates that claim 6 is rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement.

Canceled claim 6 was directed to a method for inhibiting release of IL-8 in cells, tissues or a body, comprising administering an agonist ligand specific to the G2A receptor. The basis of the rejection, as alleged by the Examiner, is that Applicants have not described with sufficient clarity all G2A receptor ligands. Not to acquiesce to the rejection, but to advance prosecution, the currently pending claims are directed to specifically enumerated G2A ligands of formulas I, II III. Applicants believe that the cancellation of claim 6 in favor of the pending claims obviates the rejection, and earnestly solicit notification to that effect.

Rejections under 35 U.S.C. § 112, second paragraph

In the Office Action, claims 24 and 25 are rejected as indefinite for reciting a use without active steps. Claims 24 and 25 have been canceled herein, thereby mooting the rejection.

Claims 6 and 11 are rejected as indefinite for allegedly being "of indeterminate scope." Claims 6 and 11 have been canceled herein, thereby mooting the rejection.

Rejection under 35 USC § 102

Claims 21-22 and 26-29 are rejected as anticipated by U.S. Patent No. 4,746,652 (Buckalew, et al.). Claims 21-22 and 26-29 have been canceled herein, thereby mooting the rejection.

Rejections under 35 USC § 103

Claims 6-18, 21-22 and 24-25 are rejected under 35 U.S.C. § 103(a) as obvious over Rikitake et al. in view of Falcone et al., in further view of U.S. Patent 6,515,001 (Saxena et al.). Applicants respectfully traverse the rejection inasmuch as it may be applied to the new claims.

As a preliminary matter, the Examiner is reminded that in order to establish a *prima facie* case of obviousness, the Examiner must show that the references (1) combine to teach or suggest all the claim limitations, (2) provide motivation to modify or combine the references, and (3) provide a reasonable expectation of success. The motivation to combine and the reasonable expectation of success must come from the references themselves, not the applicants' disclosure. *See In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). As explained below, Applicants respectfully assert that a *prima facie* case of obviousness has not been established.

The Office Action states that Rikitake teach that G2A is a high affinity receptor for LPC. The Office Action further states that Falcone et al. teach that chemokines act on target cells through G protein coupled receptors and that the engagement of a G protein coupled receptor with an agonist results in a "panoply of possible functional cellular responses." The Office Action further states that Saxena et al. teach that IL-8 is involved in inflammatory conditions and that IL-8 and its receptor CXCR-2 are expressed on macrophages in atherosclerosis in mice.

Applicants respectfully assert that the cited references, whether taken alone or in combination, do not teach or suggest the elements of the claimed invention. At most, the references establish that LPC binds the G2A receptor. Applicants concede that this was known prior to Applicants' invention. (See, e.g., Specification at page 6). However, the references do not teach or suggest administering an effective amount of an LPC compound, an SPC compound or an ether derivative of LPC to treat of a disease or disorder associated with suppression of neutrophil apoptosis or excessive release of IL-8, as recited in claim 30. Indeed, the references do not even suggest administering LPC, SPC or ether derivatives thereof for any reason. The only reference that even mentions LPC, Rikitake et al., merely reports that: 1) LPC is associated with development of atherosclerotic lesions; and 2) immunohistochemistry showed the G2A receptor is expressed on macrophages within atherosclerotic lesions. Thus, although Rikitake et al. observe endogenous LPC in a pathologic condition, this reference suggests absolutely nothing that would lead one of skill in the art to administer LPC.

Moreover, none of the cited references provide motivation to combine or modify their teachings, or a reasonable expectation of success with respect to the claimed invention. The

Examiner posits that the combination of Falcone et al. and Rikitake et al. leads the skilled artisan to use a G2A receptor agonist to suppress excessive release of IL-8, and that one of skill in the art would be motivated to combine these references, apparently because both teach that engaging G-protein coupled receptors results in "functional cellular responses," such as an increase in intracellular calcium concentration. (See Office Action at page 13). This explanation, however, fails to explain why or how one of skill in the art would identify any particular "functional cellular response" as a target in the treatment of the conditions recited in the claims. Consequently, none of the references provide any indication that the presently claimed methods would be successful, as taught by Applicants. As such, the references can at best be considered merely an invitation to experiment, which is insufficient for a finding of obviousness.

The Examiner states that Falcone and Saxena "express that which is naturally and necessarily occurring i.e. LPC effects mediated via the IL-8 receptor pathway." Even if this were a correct characterization of the teaching of the references (which Applicants do not concede), the presently claimed invention relates in one aspect to the suppression of excessive release of IL-8 by administration of LPC, which is not related to the IL-8 receptor pathway.

Accordingly, not one reference cited in the Office Action, nor the combination of references, teaches or suggests that administration of LPC, SPC or ether derivatives thereof can prevent or treat diseases associated with excessive release of IL-8 or suppression of neutrophil apoptosis, as recited in present claim 30 (or, by definition, the dependent claims). Moreover, the specific compounds recited in claim 31 and 32 are not taught by the references, and the Examiner has not shown how administration of these compounds would be obvious over the references.

For at least the above reasons, Applicants request that rejection under 35 U.S.C. § 103(a) be withdrawn.

Double patenting rejection

The Office Action includes a rejection of claims 6-18, 21-22 and 24-25 on the grounds of non-statutory double patenting over U.S. Application Serial No. 10/475,814. The Office Action states that the present Application and cited application claim treating a disease associated with inflammation with LPC and a composition comprising LPC. Applicants respectfully traverse the rejection.

U.S. Application Serial No. 10/475,814 is directed to treating sepsis with LPA and does not mention, much less claim, treating any condition with LPC, SPC or ether derivatives.

Accordingly, the rejection is improper and Applicants respectfully request withdrawal of the rejection.

CONCLUSION

As the application is now in condition for allowance, Applicants respectfully request withdrawal of the rejections and allowance of the claims. Applicants invite the Examiner to contact the undersigned should further clarification concerning this response be required.

Respectfully submitted,

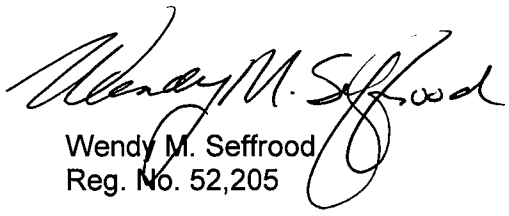

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EXHIBIT 1

Prevention (medical)

From Wikipedia, the free encyclopedia

In medicine, **prevention** is any activity which reduces the burden of mortality or morbidity from disease. This takes place at primary, secondary and tertiary prevention levels.

Primary prevention avoids the development of a disease. Most population-based health promotion activities are primary preventative measures. Secondary prevention activities are aimed at early disease detection, thereby increasing opportunities for interventions to prevent progression of the disease and emergence of symptoms. Tertiary prevention reduces the negative impact of an already established disease by restoring function and reducing disease-related complications.

See also

- Preventive medicine

Retrieved from "http://en.wikipedia.org/wiki/Prevention_%28medical%29"

Categories: Medicine stubs | Medical terms | Prevention